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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BARNHART, LORA ELIZABETH	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 06/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/642,664	FERRARA ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/17/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The examiner notes the cancellation of claims 1-7 and the addition of claims 11-15. The examiner agrees that the new claims are supported by the specification as filed.

Examination will continue at this point on claims 8-15.

Priority

The status of the parent case(s) should be updated.

Specification

Applicant is reminded of the proper content, language, and format of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and **should include that which is new in the art to which the CLAIMED invention pertains**. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) **if a mixture, its ingredients**;
(5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

The abstract should be in **narrative form** and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract

on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. **It should avoid using phrases which can be implied**, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Claim Objections

Claim 8 is objected to because of the following informalities: The word "angiogenesis" is misspelled at line 5. Claim 15 is objected to because of the following informalities: The word "endothelial" is misspelled at line 2. Appropriate correction is required.

Additionally, the examiner suspects that the word "with" at line 3 of claim 10 should recite "within".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-10 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8-10 recite the abbreviation "HGF" without particularly pointing out within the claim the basis for said abbreviation. Clarification is required.

Claims 8 and 10 are further indefinite in that they recite compositions effective for "enhancing angiogenesis", but they do not point out the level of enhancement that is

encompassed by or excluded by the claims. It is not clear which aspect or aspects of angiogenesis are claimed to be enhanced. Clarification is required.

Claim 14 recites "conditions **associated with** vascular disease" but does not particularly point out a link between the recited conditions and any vascular disease. Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8-12 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Gohda et al. (1991, U.S. Patent 5,004,805; reference A). The claims are presumably drawn to compositions comprising a pharmaceutical composition that itself comprises hepatocyte growth factor (HGF) as an active agent. In some dependent claims, the composition is in a specific package or included with various written material. In some dependent claims, HGF is in a pharmaceutical carrier comprising a buffer. In some dependent claims, the composition further comprises a pharmacologic agent used to treat conditions associated with vascular disease.

U.S. '805 teaches human HGF in a buffer comprising 0.1M sodium phosphate, pH 7.1, in 2mL test tubes (Example 2).

Regarding claims 8-10, M.P.E.P. § 2112.01 recites, "Where the only difference between a prior art product and a claimed product is printed matter that is not

functionally related to the product, the content of the printed matter will not distinguish the claimed product from the prior art." See *In re Ngai* and *In re Gulack* (citations omitted). The recited labels and written instructions in claims 8-10 have not been given patentable weight in the determination of the patentability of the product.

Claims 8-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Jardieu (1993, U.S. Patent 5,227,158; reference AA on 10/17/03 IDS) taken in light of Rosen et al. (1993, reference CR on 10/17/03 IDS) and Zarnegar et al. (1993, reference DE on 10/17/03 IDS). The claims are drawn to compositions as described above. In some dependent claims, the HGF is recombinant.

U.S. '158 teaches active recombinant human HGF in a buffer that is appropriate for administration to hepatocytes (Example, columns 9 and 10).

M.P.E.P. § 2112 reads, "The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable." Something that is old does not become patentable upon the discovery of a new property, use, or application. The discovery that HGF has a pro-angiogenic activity would not make HGF itself patentable. Rosen et al. and Zarnegar et al. are cited as evidence that HGF was known at the time the invention was made to promote angiogenesis *in vivo.*

Regarding claims 8-10, M.P.E.P. § 2112.01 recites, "Where the only difference between a prior art product and a claimed product is printed matter that is not functionally related to the product, the content of the printed matter will not distinguish the claimed product from the prior art." See *In re Ngai* and *In re Gulack* (citations

omitted). The recited labels and written instructions in claims 8-10 have not been given patentable weight in the determination of the patentability of the product.

Because the claims do not specifically define which "conditions" are associated with "vascular disease", the examiner has interpreted this limitation as broadly as reasonably possible. The composition of U.S. '805 comprises buffers and salts, which are effective for treating dehydration associated with exercise intended to prevent vascular disease.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. '805 taken in view of Unger et al. (1993, U.S. Patent 5,244,460; reference B) and Rosen et al. (1993, reference CR on IDS). The claims are drawn to compositions as described above. In some dependent claims, the pharmacological agent is vascular endothelial growth factor (VEGF).

As detailed above, U.S. '805 teaches human HGF in a pharmaceutically acceptable buffer. U.S. '805 does not teach a composition comprising both HGF and VEGF.

U.S. '460 teaches a composition comprising VEGF in a saline solution acceptable for injection into dog coronary arteries (Example 1).

Rosen et al. is cited as evidence that HGF was known to induce angiogenesis *in vivo* at the time the invention was made (see, for example, the Abstract).

A person of ordinary skill in the art would have had a reasonable expectation of success in combining the pharmaceutically acceptable VEGF composition of U.S. '460 with the pharmaceutically acceptable HGF composition of U.S. '805 because both HGF and VEGF are disclosed as being stable and active in pharmaceutically acceptable buffers. The skilled artisan would have been motivated to make said combination for the

expected benefit that administering a combination two molecules with similar activity often results in a stronger effect than would be obtained by administering either alone.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to make a pharmaceutical composition comprising both HGF and VEGF because HGF and VEGF were both known at the time the invention was made to promote angiogenesis.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

No claims are allowed. No claims are free of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Friday, 8:00am - 4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Irene Marx

IRENE MARX
PRIMARY EXAMINER

Lora E Barnhart

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